

In The Specification:

At page 6, lines 7-19, please amend the paragraph as follows:

--In one embodiment, Z is cyclohexyl, piperidinyl or N(C₁₋₆ alkyl)-piperidinyl, ~~hexahydrothiopyranyl~~, azepanyl, methylazepanyl, N(C₁₋₆ alkyl)-piperidinylmethyl, tetrahydropyranyl, piperidinylmethyl, pyridinyl, pyridinylmethyl, tetrahydrothiopyranyl, dioxolanylmethyl or dioxanylmethyl which in each case is unsubstituted or substituted by one or more substituent independently chosen from halogen, nitro, nitroso, SO₃Rf, SO₂Rf, PO₃RcRd, CONRgRh, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₂₋₆ alkenyl, C(O)C₂₋₆ alkynyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C(O)NHRf, C₃₋₁₀ heterocycle, hydroxyl, NRgRh, C(O)ORf, cyano, azido, amidino or guanido;--

At page 6, beginning at line 29, please amend the paragraph as follows:

--In a further embodiment, Z is cyclohexyl, piperidinyl, N(C₁₋₆ alkyl)-piperidinyl, ~~hexahydrothiopyranyl~~, azepanyl, methylazepanyl, N(C₁₋₆ alkyl)-piperidinylmethyl, tetrahydropyranyl, piperidinylmethyl, pyridinyl, pyridinylmethyl, tetrahydrothiopyranyl, dioxolanylmethyl or dioxanylmethyl which in each case is unsubstituted or substituted by one or more substituent independently chosen from halogen, SO₂Rf, PO₃RcRd, CONRgRh, C₁₋₆ alkyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C(O)NHRf, C₃₋₁₀ heterocycle, hydroxyl, NRgRh, C(O)ORf, cyano, azido, amidino or guanido;--

At page 7, beginning at line 12, please amend the paragraph as follows:

--In one embodiment, Z is cyclohexyl, piperidinyl, N(C₁₋₆ alkyl)-piperidinyl, ~~hexahydrothiopyranyl~~, azepanyl, methylazepanyl, N(C₁₋₆ alkyl)-piperidinylmethyl, tetrahydropyranyl, piperidinylmethyl, pyridinyl, pyridinylmethyl, tetrahydrothiopyranyl, dioxolanylmethyl or dioxanylmethyl which in each case is unsubstituted or substituted by one or more substituent independently chosen from halogen, SO₂Rf, CONRgRh, C₁₋₆ alkyl, C₆₋₁₂

aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C(O)C₁₋₆ alkyl, C(O)NHRf, C₃₋₁₀ heterocycle, hydroxyl, NRgRh, C(O)Orf or cyano;--

At page 20, lines 9-11, please amend the paragraph as follows:

--**Compound 37** 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-OXO-
~~TETRAHYDRO-HEXAHYDRO~~-THIOPYRAN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-
2-CARBOXYLIC ACID;--

At page 21, lines 7-8, please amend the paragraph as follows:

--**Compound 47** 3-[(4-~~HYDROXY~~METHYL-CYCLOHEXANECARBONYL)-
(4-METHYL-CYCLOHEXYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC
ACID;--

At page 23, lines 1-3, please amend the paragraph as follows:

--**Compound 68** 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-OXO-
~~TETRAHYDRO-HEXAHYDRO~~-THIOPYRAN-4-YL)-AMINO]-5-PHENYL-
THIOPHENE-2-CARBOXYLIC ACID;--

At page 103, beginning at line 14, please amend the paragraph as follows:

--3-[(*trans*-4-Methyl-cyclohexanecarbonyl)-(tetrahydro-thiopyran-4-yl)-amino]-5-phenyl-
thiophene-2-carboxylic acid **Compound 34**, 3-[(1,1-Dioxo- tetrahydro-~~hexahydro~~-thiopyran-
4-yl)-(*trans*-4-methyl-cyclohexanecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid
Compound 37, and Step VII: 3-[(*trans*-4-Methyl-cyclohexanecarbonyl)-(1-oxo- tetrahydro
~~hexahydro~~ -1 λ^4 -thiopyran-4-yl)-amino]-5-phenyl-thiophene-2-carboxylic acid
Compound 68.--

From page 105, line 1 to page 106, line 25, please amend the paragraphs as follows:

--Step IV

To a ice-cold stirred solution of 3-[(*trans*-4-methyl-cyclohexanecarbonyl)-(tetrahydro-thiopyran-4-yl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (119 mg, 0.26 mmol) from step 2 in DCM (1.0 mL) was added *m*-chloroperbenzoic acid (90 mg, 60%, 0.312 mmol) in one portion, and stirred for 1h. Reaction mixture was then diluted with DCM, washed with saturated aq. NaHCO₃, brine, dried and concentrated. Purification of the residue on preparative TLC using 50% EtOAc-hexane as an eluent gave 3-[(1,1-dioxo-tetrahydro~~hexahydro~~-thiopyran-4-yl)-(trans-4-methyl-cyclohexanecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (88 mg, 69%) as a white solid. NMR ¹H (CDCl₃, 400 MHz): 7.68-7.6 (m, 2H), 7.5-7.4 (m, 3H), 7.03 (s, 1H), 4.96-4.84 (m, 1H), 3.86 (s, 3H), 3.28-2.94 (m, 4H), 2.36-1.2 (m, 11H), 0.776 (d, J=4.8, 3H), 0.76-0.54 (m, 2H).

Step V

Hydrolysis of 3-[(1,1-dioxo-tetrahydro~~hexahydro~~-thiopyran-4-yl)-(4-methyl-cyclohexanecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (47 mg, 0.095 mmol) with LiOH was carried out as described for example 25, step 7 gave 3-[(1,1-dioxo-tetrahydro~~hexahydro~~-1 lambda*6*-thiopyran-4-yl)-(trans-4-methyl-cyclohexanecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid (Compound 37) (38 mg, 84%). NMR ¹H (CD₃OD, 400 MHz): 7.697 (d, J=7.17, 2H), 7.426 (t, 2H), 7.35 (t, 1H), 7.23 (s, 1H), 4.72 (brt, 1H), 3.4-3.26 (m, 2H), 3.3-2.54 (m, 2H), 2.48-2.14 (m, 4H), 1.96-1.2 (m, 8H), 0.76-0.56 (m, 2H), 0.776 (d, J=6.6, 3H).

Step VI

To a stirred solution of 3-[(*trans*-4-methyl-cyclohexanecarbonyl)-(tetrahydro-thiopyran-4-yl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (57 mg, 0.124 mmol) in EtOH (1.2 mL) from step 2 was added magnesium monoperoxyphthalic acid (29.6 mg, 0.06 mmol) in one portion, stirred for 24 h. Reaction mixture was diluted with water, extracted with EtOAc. The combined organic solution was washed with brine, dried, and concentrated. Purification of the residue on Preparative TLC using 5% MeOH-DCM gave 3-[(*trans*-4-methyl-cyclohexanecarbonyl)-(1-oxo-tetrahydro~~hexahydro~~-1 lambda*4*-thiopyran-4-yl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (30 mg, 51%). NMR ¹H (CDCl₃, 400 MHz, For major isomer): 7.66-7.6 (m, 2H), 7.5-7.4 (m, 3H), 7.09 (s, 1H), 4.84-4.76 (t, 1H), 3.85 (s,

3H), 3.4-1.2 (m), 0.772 (d, J=6.6, 3H), 0.74-0.56 (m, 2H).

Step VII

Hydrolysis of 3-[(*trans*-4-methyl-cyclohexanecarbonyl)-(1-oxo- ~~tetrahydro-hexahydro~~-11lambda*4*-thiopyran-4-yl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (30 mg, 0.063 mmol) with LiOH was carried out as described for example 25, step 7 gave 3-[(*trans*-4-methyl-cyclohexanecarbonyl)-(1-oxo- ~~tetrahydro-hexahydro~~-11lambda*4*-thiopyran-4-yl)-amino]-5-phenyl-thiophene-2-carboxylic acid (Compound 68) (15 mg, 51.8%). NMR ¹H (CD₃OD, 400 MHz, For major isomer): 7.76-7.7 (m, 2H), 7.5-7.38 (m, 3H), 7.39 (s, 1H), 4.74-4.56 (m, 1H), 3.5-1.2 (m), 0.782 (d, J=6.4, 1H), 0.75-0.55 (m, 2H).--

At page 131, in the table, third cell in the right hand column, please amend the text as follows:

--3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1,1-DIOXO- TETRAHYDRO
~~HEXAHYDRO~~-THIOPYRAN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID--

At page 133, in the table, second cell in the right hand column, please amend the text as follows:

--3-[(4- HYDROXYMETHYL-CYCLOHEXANECARBONYL)-(4-METHYL-CYCLOHEXYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID--

At page 137, in the table, first cell in the right hand column, please amend the text as follows:

--3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-OXO- TETRAHYDRO
~~HEXAHYDRO~~-THIOPYRAN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID--